the Rockefeller group's linkage of these enzymes with the mitochondrion. He later wrote, "The mitochondrion and the cyclophorase system thus turned out to be the structural and functional sides of the same unit" (Green, 1957–8, p. 178). He nonetheless advocated using the name "cyclophorase system" "for the functional attributes of the same entity" (1951b, p. 19, n. 2). Green credited Harman (1950a), who was working with him at the Enzyme Institute, with establishing the proportionality of cyclophorase activity and the presence and number of mitochondria.

An important aspect of Green's conception of the cyclophorase system was that it not only linked together the enzymes but also bound them to the coenzymes that figured in the reactions. Washing the preparation would remove the coenzymes and, as well, most of the NAD, NADP, FAD, and ATP in the cell that was normally bound in the cyclophorase system. Green proposed further that a coenzyme was bound as a *prosthetic group* to the protein component of an enzyme, which he referred to as the *apoenzyme*, and that when the two were split, the enzyme was modified. Green suggested that such an arrangement was most efficient in that it required only one coenzyme molecule per enzyme molecule, whereas if they were dissociated and relied on random processes such as diffusion to encounter each other, many times more coenzyme molecules would be required. Green did note a serious problem posed by binding of the coenzyme to the enzyme:

> . . . pyridinenucleotide must be capable not only of being reducible by the substrate of the oxidase with which the former is combined, but also in its reduced form has to interact with the flavin prosthetic group of diaphorase – the enzyme which catalyses the oxidation of dihydropyridinenucleotide by one of the cytochrome components. When the pyridinenucleotide is free as in the case of the classical, soluble systems, this sequence of reactions poses no difficulty. The coenzyme is free to shuttle back and forth . . . In the cyclophorase system with bound pyridinenucleotide, the extent of shifting back and forth is severely limited. Some mechanism must be invoked to explain how a coenzyme fixed in a rigid structure would be capable of interacting with a variety of systems. (1951a, p. 429)

Most biochemists rejected Green's cyclophorase proposal as an excessively speculative response to the difficulty of rendering the enzymes of oxidative metabolism soluble and isolating them. Nonetheless, like Lehninger, those biochemists working on oxidative phosphorylation in the early 1950s came to recognize, if only as a nuisance factor, that the enzymes of oxidative phosphorylation were localized in the mitochondrion and in some intimate way connected with mitochondrial membranes. The question was how. The next